



X-linked thrombocytopenia

X-linked thrombocytopenia is a bleeding disorder that primarily affects males. This condition is characterized by a blood cell abnormality called thrombocytopenia, which is a shortage in the number of cells involved in clotting (platelets). Affected individuals often have abnormally small platelets as well, a condition called microthrombocytopenia. X-linked thrombocytopenia can cause individuals to bruise easily or have episodes of prolonged bleeding following minor trauma or even in the absence of injury (spontaneous bleeding). Some people with this condition experience spontaneous bleeding in the brain (cerebral hemorrhage), which can cause brain damage that can be life-threatening.

Some people with X-linked thrombocytopenia also have patches of red, irritated skin (eczema) or an increased susceptibility to infections. In severe cases, additional features can develop, such as cancer or autoimmune disorders, which occur when the immune system malfunctions and attacks the body's own tissues and organs. It is unclear, however, if people with these features have X-linked thrombocytopenia or a more severe disorder with similar signs and symptoms called Wiskott-Aldrich syndrome.

Some people have a mild form of the disorder called intermittent thrombocytopenia. These individuals have normal platelet production at times with episodes of thrombocytopenia.

Frequency

The estimated incidence of X-linked thrombocytopenia is between 1 and 10 per million males worldwide; this condition is rarer among females.

Genetic Changes

Mutations in the *WAS* gene cause X-linked thrombocytopenia. The *WAS* gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling activates the cell when it is needed and triggers its movement and attachment to other cells and tissues (adhesion). In white blood cells, which protect the body from infection, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

WAS gene mutations that cause X-linked thrombocytopenia typically lead to the production of an altered protein. The altered WASP has reduced function and cannot efficiently relay signals from the cell membrane to the actin cytoskeleton. In people with X-linked thrombocytopenia, these signaling problems primarily affect platelets, impairing

their development. In some cases, white blood cells are affected. When WASP function is impaired in white blood cells, they are less able to respond to foreign invaders and immune problems such as infections, eczema, and autoimmune disorders can occur.

Inheritance Pattern

This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell may or may not cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases of X-linked inheritance, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- thrombocytopenia 1
- XLT

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Thrombocytopenia, X-linked
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1839163/>

Other Diagnosis and Management Resources

- GeneReview: WAS-Related Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1178>
- National Heart Lung and Blood Institute: How is Thrombocytopenia Treated?
<https://www.nhlbi.nih.gov/health/health-topics/topics/thcp/treatment>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>

- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Thrombocytopenia
<https://medlineplus.gov/ency/article/000586.htm>
- Health Topic: Platelet Disorders
<https://medlineplus.gov/plateletdisorders.html>

Genetic and Rare Diseases Information Center

- X-linked thrombocytopenia
<https://rarediseases.info.nih.gov/diseases/5176/x-linked-thrombocytopenia>

Additional NIH Resources

- National Heart Lung and Blood Institute: How is Thrombocytopenia Treated?
<https://www.nhlbi.nih.gov/health/health-topics/topics/thcp/treatment>
- National Heart Lung and Blood Institute: What is Thrombocytopenia?
<https://www.nhlbi.nih.gov/health/health-topics/topics/thcp/>

Educational Resources

- Cleveland Clinic
<http://my.clevelandclinic.org/health/articles/thrombocytopenia>
- CLIMB Information Sheet
<http://www.climb.org.uk/IMD/Tango/Thrombocytopenia.pdf>
- Disease InfoSearch: Thrombocytopenia, x-linked
<http://www.diseaseinfosearch.org/Thrombocytopenia%2C+x-linked/7084>
- Johns Hopkins Medicine: What are Platelets and Why are They Important?
http://www.hopkinsmedicine.org/heart_vascular_institute/clinical_services/centers_excellence/womens_cardiovascular_health_center/patient_information/health_topics/platelets.html
- Merck Manual Consumer Version: Thrombocytopenia
<http://www.merckmanuals.com/home/blood-disorders/platelet-disorders/overview-of-thrombocytopenia>

- Monroe Carell Jr. Children's Hospital at Vanderbilt: Overview of Blood and Blood Components
<http://childrenshospital.vanderbilt.org/library/article.php?term=b&ContentTypeId=90&ContentId=P02316&Category=SearchTitle&SubtopicId=&lang=en§ion=33153>
- Orphanet: X-linked thrombocytopenia with normal platelets
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=852

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
<http://www.climb.org.uk/>
- National Organization for Rare Disorders (NORD): WAS Related Disorders
<https://rarediseases.org/rare-diseases/was-related-disorders/>
- Platelet Disorder Support Association: Platelet Details
<https://www.pdsa.org/about-its/platelet-details.html>
- The Wiskott-Aldrich Foundation
<http://www.wiskott.org/>

GeneReviews

- WAS-Related Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1178>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22X-linked+thrombocytopenia%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28x-linked+thrombocytopenia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- THROMBOCYTOPENIA 1
<http://omim.org/entry/313900>

Sources for This Summary

- Albert MH, Bittner TC, Nonoyama S, Notarangelo LD, Burns S, Imai K, Espanol T, Fasth A, Pellier I, Strauss G, Morio T, Gathmann B, Noordzij JG, Fillat C, Hoenig M, Nathrath M, Meindl A, Pagel P, Wintergerst U, Fischer A, Thrasher AJ, Belohradsky BH, Ochs HD. X-linked thrombocytopenia (XLT) due to WAS mutations: clinical characteristics, long-term outcome, and treatment options. *Blood*. 2010 Apr 22;115(16):3231-8. doi: 10.1182/blood-2009-09-239087. Epub 2010 Feb 19.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20173115>
- Andreu N, Matamoros N, Escudero A, Fillat C. Two novel mutations identified in the Wiskott-Aldrich syndrome protein gene cause Wiskott-Aldrich syndrome and thrombocytopenia. *Int J Mol Med*. 2007 May;19(5):777-82.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17390083>
- Bourne HC, Weston S, Prasad M, Edkins E, Benson EM. Identification of WASP mutations in 10 Australian families with Wiskott-Aldrich syndrome and X-linked thrombocytopenia. *Pathology*. 2004 Jun;36(3):262-4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15203732>
- Imai K, Morio T, Zhu Y, Jin Y, Itoh S, Kajiwarra M, Yata J, Mizutani S, Ochs HD, Nonoyama S. Clinical course of patients with WASP gene mutations. *Blood*. 2004 Jan 15;103(2):456-64. Epub 2003 Sep 11.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12969986>
- Jin Y, Mazza C, Christie JR, Giliani S, Fiorini M, Mella P, Gandellini F, Stewart DM, Zhu Q, Nelson DL, Notarangelo LD, Ochs HD. Mutations of the Wiskott-Aldrich Syndrome Protein (WASP): hotspots, effect on transcription, and translation and phenotype/genotype correlation. *Blood*. 2004 Dec 15;104(13):4010-9. Epub 2004 Jul 29.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15284122>
- Lee WI, Huang JL, Jaing TH, Wu KH, Chien YH, Chang KW. Clinical aspects and genetic analysis of taiwanese patients with wiskott-Aldrich syndrome protein mutation: the first identification of x-linked thrombocytopenia in the chinese with novel mutations. *J Clin Immunol*. 2010 Jul;30(4):593-601. doi: 10.1007/s10875-010-9381-x. Epub 2010 Mar 16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20232122>
- Notarangelo LD, Notarangelo LD, Ochs HD. WASP and the phenotypic range associated with deficiency. *Curr Opin Allergy Clin Immunol*. 2005 Dec;5(6):485-90. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16264326>

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